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EXAMINER	
RAWLINGS, STEPHEN L	
ART UNIT	**PAPER NUMBER**
1643	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	02/14/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	09/776,865	HELLERQVIST, CARL G.	
	Examiner	Art Unit	
	Stephen L. Rawlings, Ph.D.	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 May 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,4-16,29-38,40-48,55 and 56* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,4-16,29-38,40-48,55 and 56* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *02 February 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. The amendment filed May 22, 2006, has been entered. Claims 1, 29, 30, 32, 35, 40, 41, 44-48, and 55 have been amended.

2. The second declaration under 37 C.F.R. § 1.132 by Carl G. Hellerqvist, Ph.D., which was filed May 22, 2006, is acknowledged and has been entered.

3. Claims 1, 4-16, 29-38, 40-48, 55, and 56 are currently under prosecution.

4. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Response to the Declaration

5. The merit of the second declaration under 37 C.F.R. § 1.132 by Carl G. Hellerqvist, Ph.D., which was filed May 22, 2006, has been carefully considered but not found persuasive or sufficient to overcome the rejection of claims 1, 4-16, 29-38, 40-48, 55, and 56 under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The reasons that the merit of the declaration has not been found persuasive or sufficient to overcome this ground of rejection, based upon the inadequacy of the supporting disclosure of the claimed invention, are further discussed below in responding to Applicant's arguments traversing the rejection, but primarily the showing provided by the declaration is not reasonably commensurate in scope with the breadth of the claims and fails to establish that the disclosure would, contrary to a preponderance of factual evidence suggesting otherwise, suffice to enable the skilled artisan to use the claimed invention to achieve the claimed effect without undue and/or unreasonable experimentation.

Ground of Rejection Maintained

Claim Rejections - 35 USC § 112

6. The rejection of claims 1, 4-16, 29-38, 40-48, 55, and 56 under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement, is maintained. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Beginning at page 8 of the response filed May 22, 2006, Applicant has traversed this ground of rejection.

Applicant's arguments have been carefully considered but not found persuasive for the following reasons:

Applicant has argued, contrary to the position of the Office, that the disclosure would satisfy the enablement requirement set forth under 35 U.S.C. § 112, first paragraph, because U.S. patent laws fail to require a rigorous correlation between animal models and the success of the claimed invention in humans.

In response, MPEP § 2164.01 states:

> The standard for determining whether the specification meets the enablement requirement was cast in the Supreme Court decision of *Mineral Separation v. Hyde*, 242 U.S. 261, 270 (1916) which postured the question: is the experimentation needed to practice the invention undue or unreasonable? That standard is still the one to be applied. *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988). Accordingly, even though the statute does not use the term "undue experimentation," it has been interpreted to require that the claimed invention be enabled so that any person skilled in the art can make and use the invention without undue experimentation. *In re Wands*, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988).

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue". These factors, which have been outlined in the Federal Circuit decision of *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988), include, but are not limited to, the nature of the invention, the state of the prior art, the relative skill of those in the art, the amount of direction or guidance disclosed in the specification, the presence or absence of working examples, the predictability or unpredictability of the art, the breadth of the claims, and the quantity of experimentation which would be required

in order to practice the invention as claimed. See also *Ex parte Forman*, 230 USPQ 546 (BPAI 1986).

Therefore, upon careful consideration of the factors used to determine whether undue experimentation is required, in accordance with the Federal Circuit decision of *In re Wands*, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988), it has been determined that the amount of guidance, direction, and exemplification disclosed in the specification, as filed, would not be sufficient to have enabled the skilled artisan to use the claimed invention at the time the application was filed without undue and/or unreasonable experimentation.

Citing *In re Brana*, 51 F.3d 1560, 1567 (Fed. Cir. 1995), Applicant has further argued a demonstration of the effectiveness of a drug is not required for obtaining a patent, and that disclosure provided in the specification would enable the skilled artisan to make and use the GBS toxin receptor compositions having an amino sequence substantially identical to the amino acid sequences of HP59 or SP55, as claimed.

In response, Applicants are required to meet the enablement requirements set forth under 35 U.S.C. § 112, first paragraph. In view of the preponderance of evidence, which has been made of record in establishing a case for the insufficiency of the specification to meet this requirement, it is not immediately apparent that these requirements would be met, and therefore Applicant has the burden of persuading the Office that given only the benefit of the instant disclosure the skilled artisan could have used the claimed invention at the time the application was filed to achieve the claimed effect without undue and./or unreasonable experimentation.

Furthermore, it is submitted that Applicant's reliance upon *In re Brana* is misplaced, as the situation faced by Applicants in the course of the instant prosecution is not analogous to that faced by Brana et al. because, in this instance, Applicant has not established the clinical utility of the claimed invention. Moreover, there is preponderance of factual evidence of record indicating that Applicant has not provided a reasonably correlative study suggesting the potential utility of the claimed invention.

Here, it is not merely a question of whether or not a favorable comparison of the claimed invention and proven effective antitumor therapeutic compounds implicitly asserts that the invention is also highly effective against cancer, or whether such a disclosure can be reasonably extrapolated to reliably predict the efficacy of the claimed invention encompassing clinical

application. Again, considering the nature of the invention, the state of the art at the time the application was filed, the level of skill in the art, the level of predictability in the art, the breadth of the claims and the amount of exemplification disclosed by Applicant in the specification, it appears that the quantity and type of experimentation that would be required, before the claimed invention might be practiced to achieve the claimed effect, should be considered undue and/or unreasonable.

Moreover, in contrast to the situation faced by Brana et al., the skilled artisan would not merely be required to perform routine experimentation using conventional methodology to determine optimally safe and effective dosages and schedules for administration in practicing the claimed invention to achieve the claimed effect. Contrary to the situation faced by Brana et al., in this instance, there does not appear to be a reasonable presumption of the utility of the claimed invention.

Applicant has argued that second declaration under 37 C.F.R. § 1.132 by Carl G. Hellerqvist, Ph.D., which was filed May 22, 2006, concludes that observations in appropriately selected mouse models reasonably correlate with the observations in other mammals, such as humans, then asserting that the mouse models used in the disclosed examples of the present application were "selected so they reasonably correlate with human pathological angiogenesis" (page 9, paragraph 2).

In response, it appears that Applicant has argued because the mouse models were *selected* for use, those mouse models necessarily "correlate with human pathological angiogenesis"; however, the claims are directed to a method for attenuating cancer in a mammal, not for attenuating pathological angiogenesis, and just because the mouse models used in the examples were deliberately chosen, rather than some other mouse models, for example, does not reasonably argue that the mouse models used provide results that may be extrapolated to reliably and accurately predict the outcome of practicing the claimed invention in a clinical setting, for example, to treat a human afflicted by any type of cancer.

The specification describes exemplary experiments in which C57 mice were immunized using a mixture of three peptide conjugates comprising fragments of the amino terminus of HP59 (i.e., Hab1, Hab2 and Hab3, as shown in Table 3), which were conjugated to keyhole limpet hemocyanin (KLH) in complete Freund's adjuvant (CFA). When a positive antibody titer for

anti-peptide antibodies was obtained from all experimental mice, the mice were challenged with mouse melanoma B16 cells or mouse Lewis lung carcinoma cells. The specification discloses, as shown in Table 6, the melanoma tumors of immunized mice were 45% smaller than those of their control counterparts and the Lewis lung tumors of immunized mice were 38% smaller than those of their control counterparts.

In contrast to these disclosures, the claims are directed to a process for attenuating any of a very large plurality of different types of cancer, *not just mouse melanoma or lung carcinoma*, and, in any mammal, *not just experimental mice.* Furthermore, the claims are directed to a process comprising administering to any such mammal an amount of one or more Group B β-hemolytic *Streptococci* (GBS) toxin receptors or immunogenic fragments thereof, *not to just a mixture of three peptide conjugates comprising fragments of the amino terminus of HP59 (i.e., Hab1, Hab2 and Hab3, as shown in Table 3), which were conjugated to keyhole limpet hemocyanin (KLH) in complete Freund's adjuvant (CFA).*

Applicant is reminded that reasonable correlation must exist between the scope of the claims and scope of enablement set forth.

In deciding *In re Fisher*, 166 USPQ 18, 24 (CCPA 1970), the Court indicated the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute. "Tossing out the mere germ of an idea does not constitute enabling disclosure. While every aspect of a generic claim certainly need not have been carried out by an inventor, or exemplified in the specification, reasonable detail must be provided in order to enable members of the public to understand and carry out the invention." *Genentech Inc. v. Novo Nordisk A/S*, 42 USPQ2d 1001, 1005 (CA FC 1997).

Given the state of the art, the level of skill in the art, and the unpredictability of the art, as evidenced by the numerous references cited in support of this rejection, and considering the vast difference in the scope of the claims and scope of the examples set forth in the application, it is submitted that the overly broad scope of the claims would merely serve as an invitation to one skilled in the art to identify an amount of one or more Group B β-hemolytic *Streptococci* (GBS) toxin receptors or immunogenic fragments thereof that can be administered to any mammal to attenuate the onset, growth and/or progression of any type of cancer in the mammal; yet,

defining a substance by its principal biological activity amounts to an alleged conception having no more specificity than that of a wish to know the identity of any material with that biological property. See *Colbert v. Lofdahl*, 21 USPQ2d 1068, 1071 (BPAI 1991).

Notably, among the many references cited to show the state of the art, the level of skill in the art, and the unpredictability of the art, Peterson et al. (of record) teaches numerous agents have show exciting activity in preclinical models and yet have had minimal activity clinically; see, e.g., the abstract. Such disappointments, Peterson et al. discloses, "have led to reasonable skeptism about the true value of both syngeneic and xenograft rodent tumour models in accurately identifying agents that will have important clinical utility" (abstract).

Schuh (of record) reviews the trials, tribulations and trends in tumor modeling in mice to disclose, for example, that "[c]ommon reliance on survival and tumor burden data in a single mouse model often skews expectations towards high remission and cure results; a finding seldom duplicated in clinical trials" (abstract). Furthermore, Schuh discloses, "[d]espite historical significance and ongoing utility, tumor models in mice used for preclinical therapeutic intervention often error towards false positive results and curing cancer in mice" (page 62, column 1).

Kelland (of record) states mouse models are of limited value, because, among other reasons, the mechanisms of action of treatment strategies, such as that disclosed in this application, rely upon the recruitment of the host's (i.e., mouse) immune response, which differs from or is not reflective of that found in man (page 834, column 2). With such limitations of the xenograft model in mind, Kelland suggests that the case for using the model within a target-driven drug development cascade need to be justified on a case-by-case basis (page 835, column 1). Still, Kelland et al. does not altogether discount the usefulness of such models, since, at present, "it is premature and too much a 'leap of faith' to jump directly from *in vitro* activity testing (or even in silico methods) to Phase I clinical trials (via preclinical regulatory toxicology)" (page 835, column 2). Notably, however, Kelland does not advocate the use of a single xenograft model to exhort one to accept assertions of the effectiveness of treating multiple and different types of cancer in any of a plurality of different mammals, including humans, using the same agent, as has been done in the instant application. Again, Kelland compels one to decide on a case-by-case basis whether such a model is suitable or not; and would not advocate

the use of the Lewis lung tumor model, for example, to predict the effectiveness of a treatment modality for other types of cancer.

As recently as August 2006, Dennis (*Nature*. 2006 Aug 7; **442**: 739-741) continues to report, despite their present indispensableness, mouse models, such as xenografts, have only limited utility in predicting the clinical effectiveness of anticancer treatments; see entire document (e.g., page 739, column 2). Dennis explains there is a "laundry list" of problems associated with the use of mice to model human diseases, such as cancer (page 739, column 1). Accordingly, Dennis reports, "[a]lthough virtually every successful cancer drug on the market will have undergone xenograft testing, many more that show positive results in mice have had little or no effect on humans, possibly because the human tumours are growing in a foreign environment" (page 740, column 1). Therefore, quoting Howard Fine, Dennis concludes: " 'Mice are valuable but they are, after all, still mice' ", suggesting the best study subject will always be the human (page 741, column 3).

Applicant has argued the declaration describes multiple studies in which Applicant demonstrated correlation of the effects of administering GBS toxin to mice and humans.

In response, it is not apparent to which studies Applicant has referred, since none of the studies described in the declaration appear to establish a correlation between the outcome of practicing the invention in mice and the outcome of practicing the invention in humans. Moreover, none of the relevant studies described in the declaration involved humans.

Applicant has argued that HP59 is present in tumor vasculature, independently of site and type.

In response, it is understood that HP59 is a human protein; it is not expressed in naturally occurring non-humans. And, contrary to Applicant's assertion, Table 1 at page 4190 of Fu et al. (2001) does not show that HP59 is present in tumor vasculature, independently of site and type; rather Fu et al. teaches human tumor tissues that stained positively for expression of HP59 (i.e., human ovarian cancer, human female breast cancer, human male breast cancer, human colon cancer, human lung cancer, and liver tumor).

Applicant has argued that HP59 is a pathologic vasculature target common among humans, sheep and mice.

In response, only humans express HP59; sheep express SP55, and it is uncertain whether the mouse ortholog of HP59 or SP55 is known and fully characterized, but mice do not express human or sheep proteins.

Applicant has argued that the declaration states that Applicant has shown that administration of HP59 generates a cellular immune response that inhibits pathological angiogenesis.

In reply, the claims are directed to a process for attenuating any of a very large plurality of different types of cancer, *not just mouse melanoma or lung carcinoma*, and, in any mammal, *not just experimental mice*. Furthermore, the claims are directed to a process comprising administering to any such mammal an amount of one or more Group B β-hemolytic *Streptococci* (GBS) toxin receptors or immunogenic fragments thereof, *not to just HP59*.

Applicant has argued that in the field of cancer vaccines, mouse models are considered to correlate reasonably well with human pathological angiogenesis conditions, such as those conditions associated with cancer.

In reply, Applicant has not provided any factual evidence to support the assertion that in the field of cancer vaccines, mouse models are considered to correlate reasonably well with human pathological angiogenesis conditions. Furthermore, it is aptly noted that the claims are directed to a process for attenuating any of a very large plurality of different types of cancer, *not pathological angiogenesis conditions associated with cancer*.

Applicant has contended that references cited in the preceding Office action to support the Office's position are irrelevant, because those references predominantly focus on the limitations of mouse models for predicting clinical outcomes during the development of drugs targeting tumor-specific targets, as opposed to pathological vasculature-specific targets.

In response, contrary to Applicant's assertion, *HP59 is a tumor-specific target antigen*, not a non-tumor specific antigen, because, while it is expressed abundantly in the vasculature of tumors, it is absent from healthy adult tissues; see, e.g., Fu et al. (2001) (of record).

Furthermore, the claims are not solely directed to processes for attenuating the onset, growth or progression of vascularized tumors, *but rather any type of cancer*. Additionally, the Examiner disagrees with Applicant's contention, as regardless of whether the antigen targeted by

immunotherapy is expressed by the cells of a vascularized tumor or its vasculature, the artisan would appreciate that many of the same limitations of mouse modeling are just as likely to apply.

As previously noted, Saijo et al. (of record) reviewed the reasons for negative phase III trial of molecular-target-based drugs and their combinations; see entire document (e.g., the abstract). Saijo et al. discloses that while numerous phase III trials have been conducted upon the basis of promising preclinical data such as that disclosed in the instant application, few have yielded strongly positive results, and the majority of results have been negative (e.g., abstract). Saijo et al. discloses that there are problems in preclinical prediction of combined effects of anticancer drugs, and the results of preclinical prediction of combined effects have been very poor (page 773, column 2). Saijo et al. teaches many reasons for the poor predictability of combined effects (page 774, Table 6), but Saijo comments such failure may occur because the molecular targets are not essential for growth, invasion, or metastasis of the tumor (paragraph bridging pages 772 and 773).

Pointedly, there is no factual evidence of record suggesting that HP59, for example, is essential for growth, invasion, or metastasis of any and all types of tumors.

Applicant has remarked that genetic and phenotypic diversity of tumor tissues makes tumor-specific targeting difficult, asserting that because the vasculature of tumors is genetically and phenotypically homogeneous, one mouse model is as good as another, and the use of any mouse model is sufficient to demonstrate the effectiveness of the claimed invention.

In response, Applicant's argument depends upon a presumption that the vasculature of tumors is genetically and phenotypically homogeneous, but Applicant has not provided reasonable factual evidence suggesting that such a presumption should be made; and to the contrary Fujiwara (*Vasc. Med.* 2006 May; **11** (2): 115-121), for example, teaches "endothelial cells (ECs), the main component of vasculature, are heterogeneous, as revealed by our phenotypic and molecular biological studies in the laboratory, and it is still hard to adequately understand the molecular mechanisms of angiogenesis and vasculogenesis" (abstract); see entire document. Similarly, Onofri et al. (*J. Endocrinol.* 2006 Oct; **191** (1): 249-261) teaches, in pituitary tumors, a heterogeneous VEGFR expression pattern was observed by immunohistochemistry; see entire document (e.g., the abstract). So, since the vasculature of

tumors is *not* homogeneous, the use of one or two mouse models is not reasonably expected to be sufficient to demonstrate the effectiveness of the claimed invention.

Accordingly, Applicant's arguments set forth in the response filed May 22, 2006, have been carefully considered but not found persuasive to overcome this ground of rejection.

It is presumed that the merit of any other of Applicant's arguments set forth as part of the amendment filed February 6, 2006, was predicated upon entry of the amendment; because the amendment was non-responsive, and thus not entered, those arguments are believed moot.

Claim Rejections - 35 USC § 112

7. The rejection of claims 1, 4-16, 29-38, 40-48, 55, and 56 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement, is maintained. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Beginning at page 12 of the response filed May 22, 2006, Applicant has traversed this ground of rejection.

Applicant's arguments have been carefully considered but not found persuasive for the following reasons:

Applicant has remarked that the claims have been amended so as to be directed to a genus of Group B β-hemolytic *Streptococci* (GBS) toxin receptors having an amino acid sequence substantially identical to HP59 or SP55 or immunogenic fragments thereof. Accordingly, because Applicant has described the amino acid sequences of HP59 and SP55, as well as more than one immunogenic fragment thereof, the written description requirement has been satisfied.

The Examiner disagrees.

Again, the considerations that are made in determining whether a claimed invention is supported by an adequate written description are outlined by the published Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112, para. 1, ``Written Description" Requirement (Federal Register; Vol. 66, No. 4, January 5, 2001; hereinafter "Guidelines"). A

copy of this publication can be viewed or acquired on the Internet at the following address: <http://www.gpoaccess.gov/>.

Claims 1, 4-16, 29-38, 40-48, 55, and 56 are directed to a genus of polypeptides that are Group B β-hemolytic *Streptococci* (GBS) toxin receptors having an amino acid sequence substantially identical to HP59 and SP55 or immunogenic fragments thereof.

At paragraph [0040] of the published application, the specification discloses:

> As applied to polypeptides, the term "substantial identity" means that two peptide sequences, when optimally aligned by the BLAST computer program, share at least about 80 percent sequence identity, at least about 86 percent sequence identity, and preferably at least about 90 percent sequence identity.

At paragraph [0041] of the published application, the specification discloses:

> The term "fragment" as used herein refers to a peptide that has an amino-terminal, internal and/or carboxy-terminal deletion, but where the remaining amino acid sequence is identical to the corresponding positions in the naturally occurring sequence deduced, for example, from a full-length DNA sequence. Fragments typically are at least about 3 amino acids long, preferably are about 5-10 amino acids long, more preferably are about 10-50 amino acids long, and even more preferably are more than about 50 amino acids long. Also preferred are fragments that comprise one or more extracellular domains of a GBS toxin receptor. Such fragments may also comprise portions of transmembrane and intracellular domains sufficient to maintain the polypeptide fragment in a stereochemical conformation on the surface of a cell, lipid membrane, liposome, micelle, or other lipophilic structure

And, at paragraph [0042] of the published application, the specification discloses:

> The singular forms "a," "an" and "the" include plural referents unless the context clearly dictates otherwise.

Therefore, given the broadest reasonable interpretation that is consistent with the specification and that which would be understood by the artisan of skill in the art, the claims are directed to a genus of structurally and/or functionally disparate polypeptides that comprise an amino acid sequence (i.e., at least two contiguous amino acids of any given sequence) that is substantially identical (i.e., at least 80% identical, as defined by the specification) to that of either HP59 (SEQ ID NO: 2) or SP55 (SEQ ID NO: 4).

While the specification describes two polypeptides, namely the polypeptides of SEQ ID NO: 2 and SEQ ID NO: 4, the specification fails to describe how these polypeptides are representative of the genus, as a whole, to which the claims are directed. Moreover, the claims

fail to recite and the specification fails to describe a particularly identifying (i.e., substantial) structural feature that is shared by the members of the genus of polypeptides to which the claims are directed, which correlates with a particularly identifying functional feature also common among members of the genus, such that it would be possible to immediately envision, recognize or distinguish at least a substantial number of those members. Therefore, the claims are directed to a genus of polypeptides that vary in substantially in both structure and function; yet, the specification only describes two such polypeptides. As such, the specification would not reasonably convey to the skilled artisan that Applicant had possession of the claimed invention at the time the application was filed.

"Guidelines" states, "[p]ossession may be shown in a variety of ways including description of an actual reduction to practice, or by showing the invention was 'ready for patenting' such as by disclosure of drawings or structural chemical formulas that show that the invention was complete, or by describing distinguishing identifying characteristics sufficient to show that the applicant was in possession of the claimed invention" (*Id.* at 1104). "Guidelines" further states, "[f]or inventions in an unpredictable art, adequate written description of a genus which embraces widely variant species *cannot* be achieved by disclosing only one species within the genus" (Id. at 1106); accordingly, it follows that an adequate written description of a genus cannot be achieved in the absence of a disclosure of at least one species within the genus. Because the claims encompass a genus of variant species, an adequate written description of the claimed invention must include sufficient description of at least a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics sufficient to show that Applicant was in possession of the claimed genus. However, factual evidence of an actual reduction to practice has not been disclosed by Applicant in the specification; nor has Applicant shown the invention was "ready for patenting" by disclosure of drawings or structural chemical formulas that show that the invention was complete; nor has Applicant described distinguishing identifying characteristics sufficient to show that Applicant had possession of the claimed invention at the time the application was filed.

As explained in the preceding Office action, the specification provides an adequate written description of nucleic acid molecules that comprise or consist of SEQ ID NO: 1, nucleic

acid molecules that comprise or consist of the *full* complement of the nucleotide sequence of SEQ ID NO: 1 or the *full* complement of a nucleotide sequence encoding the amino acid sequence of SEQ ID NO: 2, nucleic acid molecules that *consist* of a polynucleotide sequence of SEQ ID NO: 1 (e.g., a nucleic acid molecule consisting of a fragment of SEQ ID NO: 1), and nucleic acid molecules that *consist* of a polynucleotide sequence that is complementary to the nucleotide sequence of SEQ ID NO: 1 (e.g., a nucleic acid molecule consisting of the full complement of a fragment of SEQ ID NO: 1).

However, the description of these few members of the claimed genus of nucleic acid molecules is not sufficient to meet the requirements of 35 USC § 112, first paragraph, since the genus embraces widely variant members and an adequate description of such cannot be achieved by describing members, which are not representative of the genus. As disclosed and claimed, the genus of nucleic acid molecules does not comprise members having a common, particularly identifying structural feature that correlates with a common functional feature shared by at least a substantial number of its members. As such, absent any of the factual evidence of an actual reduction to practice discussed above, the skilled artisan could not immediately envision, recognize, or distinguish at least a substantial number of the members of the claimed genus said at least substantial number. Accordingly, the specification would not reasonably convey to the skilled artisan that Applicant had possession of the claimed invention at the time the application was filed.

In addition, the Federal Circuit has decided that a patentee of a biotechnological invention cannot necessarily claim a genus after only describing a limited number of species because there may be unpredictability in the results obtained from species other than those specifically enumerated. See *Noelle v. Lederman*, 69 USPQ2d 1508 1514 (CA FC 2004) (citing *Enzo Biochem II*, 323 F.3d at 965; *Regents*, 119 F.3d at 1568).

Furthermore, "generalized language may not suffice if it does not convey the detailed identity of an invention." *University of Rochester v. G.D. Searle Co.*, 69 USPQ2d 1886 1892 (CAFC 2004). In this instance, there is no language that adequately describes with the requisite particularity the genus of a genus of polypeptides that are Group B β-hemolytic *Streptococci* (GBS) toxin receptors having an amino acid sequence substantially identical to HP59 and SP55 or immunogenic fragments thereof, which can be used to achieve the claimed effect. A

description of what a material does, rather than of what it is, does not suffice to describe the claimed invention.

While the written description requirement can by satisfied without an actual reduction to practice, the disclosure of a catalog of potentially effective substances (i.e., any polypeptide having an amino acid sequence that is substantially identical to the amino acid sequence of HP59 or SP55) that might be found to be useful in practicing the claimed invention to achieve the claimed effect does not fulfill the written description requirement. The Federal Circuit has decided that a generic statement that defines a genus of substances by *only* their functional activity, i.e., the ability to attenuate cancer in a mammal when administered to the mammal, does not provide an adequate written description of the genus. See *The Reagents of the University of California v. Eli Lilly*, 43 USPQ2d 1398 (CAFC 1997). The Court indicated that while applicants are not required to disclose every species encompassed by a genus, the description of a genus is achieved by the recitation of a precise definition of a representative number of members of the genus, such as by reciting the structure, formula, chemical name, or physical properties of those members, rather than by merely reciting a wish for, or even a plan for obtaining a genus of molecules having a particular functional property. The recitation of a functional property alone, which must be shared by the members of the genus, is merely descriptive of what the members of genus must be capable of doing, not of the substance and structure of the members.

Although *Lilly* related to claims drawn to genetic material, the statute applies to all types of inventions. "Regardless whether a compound is claimed *per se* or a method is claimed that entails the use of the compound, the inventor cannot lay claim to the subject matter unless he can provide a description of the compound sufficient to distinguish infringing compounds from non-infringing compounds, or infringing methods from non-infringing methods". *University of Rochester v. G.D. Searle Co.*, 69 USPQ2d 1886 1894 (CAFC 2004). The claimed method depends upon finding the polypeptide having an amino acid sequence that is substantially identical to the amino acid sequence of HP59 or SP55 that may be used in practicing the claimed process to achieve the claimed effect; without such a polypeptide, it is impossible to practice the invention.

In addition, although the skilled artisan could potentially identify polypeptides (i.e., Group B β-hemolytic *Streptococci* (GBS) toxin receptors having an amino acid sequence substantially identical to HP59 and SP55 or immunogenic fragments thereof) that might be used in practicing the claimed invention by screening for candidate polypeptides that are capable of attenuating cancer in a mammal, it is duly noted that the written description provision of 35 U.S.C § 112 is severable from its enablement provision; and adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it.

> The purpose of the "written description" requirement is broader than to merely explain how to "make and use"; the applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the "written description" inquiry, *whatever is now claimed.*

Vas-Cath, Inc. v. Mahurkar, 935 F.2d 1555, 1563-64, 19 USPQ2d 1111, 1117 (CAFC 1991). See *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (CAFC 1993); *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016 (CAFC 1991); *University of Rochester v. G.D. Searle Co.*, 69 USPQ2d 1886 1892 (CAFC 2004).

Claim Rejections - 35 USC § 102

8. The rejection of claims 29-34, 37, 38, 40-43, 45-48, 55, and 56 under 35 U.S.C. 102(e), as being anticipated by U.S. Patent No. 6,803,448 B1, is maintained.

As explained in the preceding Office action, the applied reference has a common assignee and a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

At page 13 of the amendment filed May 22, 2006, Applicant has remarked that a Petition for Unintentionally Delayed Claim of Benefit for Earlier Filing Date has been filed to permit a claim to the benefit of the earlier filing date of Application No. 10/823,506, and that upon the

granting of Applicant's petition, U.S. Patent No. 6,803,448 B1 will not be prior art under § 102(e).

Applicant's remarks have been carefully considered but the Petition has been dismissed.

Double Patenting

9. The rejection of claims 29-32, 38, 40-43, 45-47, and 55 under the judicially created doctrine of obviousness-type double patenting, as being unpatentable over claims 1-11 of U.S. Patent No. 6,803,448 B1, is maintained.

At page 15 of the amendment filed May 22, 2006, Applicant has remarked that a terminal disclaimer will be filed, if appropriate.

10. Again, as previously noted, claims 29-32, 38, 40-43, 45-47, and 55 are directed to an invention not patentably distinct from claims 1-11 of commonly assigned U.S. Patent No. 6,803,448 B1. Specifically, although the conflicting claims are not identical, they are not patentably distinct from each other for the reasons set forth above in the obviousness-type double patenting rejection of claims 29-32, 38, 40-43, 45-47, and 55.

The U.S. Patent and Trademark Office normally will not institute an interference between applications or a patent and an application of common ownership (see MPEP § 2302). Commonly assigned U.S. Patent No. 6,803,448 B1, discussed above, would form the basis for a rejection of the noted claims under 35 U.S.C. 103(a) if the commonly assigned case qualifies as prior art under 35 U.S.C. 102(f) or (g) and the conflicting inventions were not commonly owned at the time the invention in this application was made. In order for the examiner to resolve this issue, the assignee is required under 35 U.S.C. 103(c) and 37 CFR 1.78(c) to either show that the conflicting inventions were commonly owned at the time the invention in this application was made or to name the prior inventor of the conflicting subject matter. Failure to comply with this requirement will result in a holding of abandonment of the application.

A showing that the inventions were commonly owned at the time the invention in this application was made will preclude a rejection under 35 U.S.C. 103(a) based upon the commonly

assigned case as a reference under 35 U.S.C. 102(f) or (g), or 35 U.S.C. 102(e) for applications filed on or after November 29, 1999.

At page 16 of the amendment filed May 22, 2006, Applicant has remarked that this requirement will be moot upon the granting of the Petition for Unintentionally Delayed Claim of Benefit for Earlier Filing Date.

Without acquiescing to Applicant's argument, the petition has been dismissed.

Conclusion

11. No claim is allowed.

12. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stephen L. Rawlings, Ph.D. whose telephone number is (571) 272-0836. The examiner can normally be reached on Monday-Friday, 8:30AM-5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms, Ph.D. can be reached on (571) 272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Stephen L. Rawlings, Ph.D.
Primary Examiner
Art Unit 1643

slr
January 31, 2007